REMARKS

Claims 34, 42, and 47 are pending in this application. Claims 34, 42, and 47 have been amended and Claims 45 and 46 are now cancelled. Claims 1-33, 35-41, 43 and 44 had been cancelled previously. Basis for the amendments to Claims 34 and 47 are found in the specification, for example, at Example 4 (page 13) and the table bridging pages 14-15. No new matter has been added. The particular Methocel and Euradgit polymers are described at *http://www.dow.com/dowexcipients/products/methocel.htm* and at *http://eudragit.evonik.com/product/eudragit/en/products-services/eudragit-products/enteric-formulations/l-30-d-55/Pages/default.aspx*, respectively.

Applicants acknowledge with thanks the interview granted by the Examiner on February 23, 2010. Participants in the telephone interview were Jo Griffith, Helen Willy, Kenneth Campbell, Vivien West, and Bonnie Deppenbrock. For Applicants, Helen Willy described the invention and the differences in the formulation of the invention as compared to Nadkarni and Staniforth formulations. The Examiner suggested that Claims 34 and 47 as written were broad and not specifically limited to the differences described as Applicants' formulation. Applicants' attorneys suggested amending the claims using language from the specification to more particularly describe the release retarding polymer and the outer coating polymer.

The Examiner has rejected Claims 34, 42, 45, and 46 under 35 U.S.C. 103(a) as being unpatentable over Nadkarni (WO 03/104192) in view of Staniforth (U.S. 5,004,614). The Examiner has concluded that it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Nadkarni and Staniforth to make a sustained release formulation of lamotrigine with an outer coat covering said core impermeable to environmental fluids even though Nadkarni and Staniforth employ different techniques for controlled release.

Applicants' Argument

The currently claimed invention is a controlled release tablet comprising a core formulation of release retarding HPMC polymer, lamotrigine and other excipients, surrounded by a coating of an enteric Eudragit polymer having at least one orifice extending through the coating.

Lamotrigine is highly soluble (17mg/ml) in the acidic environment of the stomach (pH 1-2) and virtually insoluble (<0.01mg/ml) in the more alkaline environment of the intestine (pH6-8).

The currently claimed formulation releases lamotrigine into the stomach from the tablet core, which contains the release retarding HPMC polymers, through the orifice(s) in the enteric coating, tightly controlling the release of lamotrigine into the environment where its solubility is at its highest. In the higher pH of the intestine (where the solubility of lamotrigine is much lower), the enteric coating dissolves and lamotrigine is released from the matrix by the erosion and reduction in size of the core (now totally exposed by the removal of the Eudragit coating) and diffusion.

When the release retarding HPMC polymer used in the current invention (Methocel E4M and K100LV) is hydrated, it has a viscosity 3000 times more viscous than the HPMC polymers used in the Nadkarni formulations. The higher viscosity HPMC polymer retards the release of lamotrigine from the core formulation by forming a gel and reducing the amount of the active ingredient available for diffusion. The lower viscosity HPMC polymers used in the Nadkarni formulations) do not retard the release of the active ingredient, but serve merely to bind the lamotrigine onto the pellets.

The slow release of lamotrigine in the stomach followed by a controlled release in the intestine is key to providing a once-daily dose of lamotrigine by overcoming the difference in the solubility of lamotrigine in these environments

with the added benefit that the absorption of lamotrigine is not affected by whether the stomach is full or not (i.e., no food effect).

In contrast, the pellets described in Nadkarni have an immediate release lamotrigine core surrounded by a polymer coating through which the lamotrigine diffuses into the stomach and then the intestine. The rate of diffusion is entirely dependent on the solubility of lamotrigine in the different pH environments within the gastric intestinal tract.

It is Applicants' position that the formulations embodied in amended Claims 34 and 47 are not obvious under 35 USC 103(a) as being unpatentable over Nadkarni (WO 03/104192) in view of Staniforth (U.S. 5,004, 614). Applicants maintain that their formulation as set forth in amended Claims 34 and 47 is different and nonobvious from that taught by a combination of the Nadkarni and Staniforth references. In amended Claims 34 and 47, Applicants have recited specifically that (i) the release retarding polymer is hydroxypropylmethylcellulose, which is a mixture of Methocel E4M and Methocel K100LV, and that (ii) the polymer of the outer coating is methacrylic copolymer of Eudragit L30 D55. Nowhere are these limitations taught or suggested in either Nadkarni or Staniforth. There is no indication in Nadkarni or Staniforth of the need for combining Applicants' two different means of obtaining controlled release absent the present specification's teachings.

Neither Nadkarni nor Staniforth appreciates Applicants' problem so, therefore, separate or together they cannot teach Applicants' solution. Neither Staniforth nor Nadkarni provides a system wherein the lamotrigine/active is released in two phases, the first phase having a slower release rate than the second. Nor does the combination of the teachings within Staniforth and Nadkarni achieve a slower first phase of release than the second because, with the impermeable coating, there can never be a second phase of release faster than the first. Nor do they suggest a reason to do so. It is only when armed with

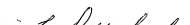
knowledge of the present invention that a person skilled in the art would attempt to assemble the invention from the two prior art references.

Therefore, the claims are not obvious in view of the combination of Nadkarni and Staniforth, for the reason that the prior art references do not teach or suggest all Applicants' claim limitations.

It is believed that the application is in condition for allowance. Therefore, reconsideration and allowance is requested.

The Commissioner is hereby authorized to charge any fees required or credit any overpayment to Deposit Account No. 07-1392.

Respectfully submitted,



Bonnie L. Deppenbrock
Attorney for Applicants
Registration No. 28,209

Date: March 12, 2010
Customer No. 23347
GlaxoSmithKline
Corporate Intellectual Property
Five Moore Drive, P.O. Box 13398
Research Triangle Park, NC 27709
Telephone: (919) 483-1577
Facsimile: (919) 483-7988